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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1801	33

DATE MAILED: 09/11/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 6-10-97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 2-7, 9, 11, 23, 27-61 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 11 is/are allowed.

☒ Claim(s) 2-7, 9, 23, 27-61 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) 07/511,430.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 32

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-409-290/40029

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on June 10, 1997 (Paper #31) has been entered.

Claims 1, 8, 10, 12,-22, and 24-26 have been cancelled. Claims 2-7, 9, 11, 23, and 27-61 are currently under examination.

Claim 7 is objected to for not reciting the identical language of the previously amended Claim 7. Claim 7 is stated to depend from Claim 1, rather than Claim 2 as set forth previously. For purposes of this examination, Claim 7 will be taken as depending from Claim 2. However, correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 27-34, 45, 48, 49, 52, 61, 2-7, and 9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. DNA that has not been isolated or purified is considered to exist in its natural state and such is not statutory subject matter. It follows then that host cells comprising this DNA are also naturally occurring.

Claims 27-60, and 7 are again rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to DNA encoding the TNF-BP described as R^2-Asp-Ser-Val-...., fragments having the ability to bind TNF, and degenerate variants of the DNA. See M.P.E.P. §§ 706.03(n) and 706.03(z). Claims 7 and 34 are directed to DNAs that hybridize to the DNA encoding TNF-BP identified in Claim 2 or 28 and encoding a protein that can bind to TNF. This DNA is beyond the scope of the disclosed Invention because there is no teaching in the specification what part of the

TNF-BP is responsible for binding to TNF. It is not predictable what part of TNF-BP binds to TNF because no structure/function studies have been done such that one of ordinary skill in the art could know that part of the TNF-BP encoded by the DNA of Claim 2 will retain TNF binding function. Therefore, it would require undue experimentation for one of ordinary skill in the art to determine that part of the TNF-BP encoded by the DNA of Claim 2 or 28 that is responsible for TNF binding. Claims 7 and 34 are also directed to any DNA encoding any TNF binding protein so long as the DNA hybridizes under low stringency with the DNA of Claim 2 or 28. The specification is non-enabling for the scope of the claimed binding proteins because the disclosure is not commensurate in scope with the Claims for the breadth of the various kinds of TNF binding proteins obtainable. This is particularly emphasized because the specification has only taught the preparation and activity of one TNF binding protein is Asp-Ser-Val-... A binding protein can be an extracellular domain of undisclosed TNF receptors, for example. There is no guidance provided in the specification as to how one of ordinary skill in the art would obtain these DNAs encoding TNF binding proteins, or what is meant by low stringency conditions. Additionally, this binding protein must antagonize TNF action at its receptor as defined on page 19 of the specification. In essence, the Claims encompass several different binding proteins for which there is insufficient enablement.

In Ex parte Hitzman (9 USPQ 2d 1821), the courts have re-emphasized that "more will be required in cases that involve unpredictable factors, such as most chemical reactions and physiological activity." It would require undue experimentation to predict and prepare the binding proteins encompassed within the scope of the Claims that possess the desired and favorable characteristics set forth in the specification, in the absence of sufficient information to predict the results with an adequate degree of certainty (*Ex parte Forman*, 230 USPQ 546).

Claims 28 (therefore 29-33), 39, 54, 55, and 57-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 28, "R_2" is not defined in the specification. Applicants may which to change this "R_2" to -- R^2 --.

In Claim 39, DNA does not have an N-terminus, or amino-terminus, and therefore it is not clear where the ATG is placed.

There is no isolation step in Claims 54, 55, and 60, and therefore it is not clear what the process is for.

In Claims 57-59, it is not clear how the TNF binding protein is modified.

Applicants argue that it is routine to screen for DNA sequences which hybridize to the DNA of Claim 2 which bind to TNF and that only time would be required. Applicants state that some experimentation would be permitted and that the Examiner has not provided evidence concerning the type of experimentation involved or any particular difficulties only skilled in the art would encounter in screening polypeptides encoded by the claimed DNA for their ability to bind to TNF. Claim 7 has now been amended so that the DNA is *encoding* and not complementary. Claim 7 now has new meaning, that is, the DNA of Claim 7 hybridizes to the DNA of Claim 2 and the DNA of Claim 7 encodes a polypeptide that binds to TNF to inhibit its action. Previously, the DNA o Claim 7 encoded no amino acid sequence and the encoding sequence was taken to be part of the DNA of Claim 2, which is an encoding sequence. Claim 7 is now much like cancelled Claim 13 and all of the previous Office Action reasons for the rejection of Claim 13 under 35 USC 112, first paragraph, (page 2) apply, especially because hybridization is at an undefined low stringency. At low

stringency conditions for hybridization the actual identity between the DNA can be very low and encode different proteins. Without guidance in the specification, one skilled in the art cannot know what the DNA which hybridizes under "low stringency" conditions to that of Claims 2 or 28, looks like. This rejection under 35 USC 112 is consistent with case law. The Courts stated in *In re Gardner* (166 USPQ 138) that: the law requires that disclosure in an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves.

Given that "fragments" have been allowed, Applicants arguments directed to "fragments" are moot.

Applicants assert that the Examiner has failed to establish that the term "low stringency" in Claim 7 is undefined. Given that this is a relative term and varies from DNA to DNA, it must by definition be undefined unless the specification sets forth the stringency conditions. This argument is not persuasive and the citation of Shimuzu et al. does not remedy the issue.

Applicants assert that conditions in which many different unrelated sequences hybridize to the DNA of Claims 2 or 28 is not what is intended by the term "low stringency" conditions. Intended or not, such is encompassed by this claim language, and the functional limitation is not enough to limit the claim to proper scope which is enabled in the specification.

Claim 11 is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.129(a) and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.129(a). Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the submission under 37 CFR 1.129(a). See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Since the fee set forth in 37 CFR 1.17(r) for a first submission subsequent to a final rejection has been previously paid, applicant, under 37 CFR 1.129(a), is entitled to have a second submission entered and considered on the merits if, prior to abandonment, the second submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a second submission and the appropriate fee for a small or large entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. If a notice of appeal and the appeal fee set forth in 37 CFR 1.17(e) were filed prior to or with the payment of the fee set forth in 37 CFR 1.17(r), the payment of the fee set forth in 37 CFR 1.17(r) by applicant will be construed as a request to dismiss the appeal and to continue prosecution under 37 CFR 1.129(a). In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is (703) 308-0034. The Examiner can normally be reached daily except alternate Fridays from 7:30 A.M. to 5:00 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Robert Wax, can be reached at (703) 308-4216. The OFFICIAL fax phone number for Group 1800 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

Karen Cochrane Carlson PhD

KAREN C. CARLSON
PATENT EXAMINER
GROUP 1800